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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/401,636	Applicant(s) HELLMAN, LARS T.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *32-33* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 25-40 are pending.

2. In view of the amendment filed 1/13/03, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 25-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for immunogenic polypeptides such as the ones shown in Fig 2 consisting of a self IgE CH3 domain from rat, human, mouse, dog or pig and one or more non-self IgE domains such as IgE CH2 domain from opossum, or platypus and IgE CH4 domain from opossum or wombat for induce anti-self IgE response in a mammal for treating atopic allergies, **does not** reasonably provide enablement for (1) *any* immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in any mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE, (2) the said immunogenic polypeptide wherein said mammal is a human, (3) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein said non-placental mammal is selected from the group consisting of opossum, platypus, koala, kangaroo, wallaby, and wombat, (4) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in any mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein said polypeptide is capable of dimerizing to

form a soluble immunogenic dimer effective to induce said anti-self IgE response in said mammal, (5) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein one of said non-self IgE domains is an IgE CH2 domain, wherein one of said non-self IgE domains is an IgE CH4 domain and wherein said self IgE CH3 domain is located between said IgE CH2 domain and said IgE CH4 domain, (6) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in any mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein one of said non-self IgE domains is an IgE CH2 domain, (7) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein one of said non-self IgE domains is an IgE CH4 domain, (8) *any* immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least N-terminal half of *any* self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in *any* non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal, (9) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least any N-terminal half of any self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in any non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in any mammal wherein the mammal is a human, (10) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least N-terminal half of *any* self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in any non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal wherein said non-placental mammal is selected from the group consisting of opossum, platypus, koala,

kangaroo, wallaby, and wombat, (11) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least any N-terminal half of *any* self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal wherein said polypeptide is capable of dimerizing to form a soluble immunogenic dimer effective to induce said anti-self IgE response in said mammal, (12) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least *any* N-terminal half of any self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal wherein one of said non-self IgE domains is an IgE CH2 domain, and (13) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least N-terminal half of *any* self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal wherein one of said non-self IgE domains is an IgE CH4 domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only immunogenic polypeptides such as the ones shown in Fig 2 comprising a self IgE CH3 domain from rat, human, mouse, dog or pig and one or more non-self IgE domains such as IgE CH2 domain from opossum, or platypus and IgE CH4 domain from opossum or wombat for induce anti-self IgE response in a mammal.

The specification does not teach how to make and use *any* immunogenic polypeptides mentioned above wherein at least one of said non-self IgE domains "comprises" *any* IgE

sequence present in *any* "non-placental mammal" for inducing anti-self IgE response because the specification discloses only IgE polypeptide such as CH2 domain from opossum, or platypus and IgE CH4 domain from opossum or wombat. Even if the non-self IgE domains (IgE sequence) are limited to the specific non-placental mammal such as opossum, platypus, and wombat, it is noted that the IgE sequence of platypus diverges from the IgE sequence (diverges) of other members of the non-placental mammal such as opossum, and wombat (See Figure 2, in particular). Thus it is clear that not all IgE sequences in non-placental mammal are similar, let alone capable of inducing anti-self IgE response in any mammal. Further, there is no disclosure about the IgE sequence from other non-placental mammal such as koala, kangaroo, and wallaby. Given the divergent of IgE sequence among the non-placental mammal, there is insufficient guidance as to the structure such as the amino acids of the IgE sequence from any other non-placental mammal such as koala, kangaroo, and wallaby.

Further, the term "comprises" is open-ended. It expands the undisclosed non-self IgE domains to include additional amino acid at either or both ends. There is no guidance in the specification as to what type and number of amino acids can be added and whether the polypeptide having extra amino acids would retain both structure and function such as stabilizes the functional conformation of the self-IgE CH3 domain since the CH3 domain is critical for IgE binding to the high affinity FcεRI. Finally, there is insufficient working example demonstrating that any undisclosed immunogenic polypeptide consisting essentially of any self IgE CH3 domain and one or more non-self IgE domains comprises any IgE sequence present in any undisclosed non-placental mammal is effective to induce an anti-self IgE response in any mammal such as human. Without sufficient guidance, the immunogenic polypeptide that would be capable of dimerizing to form a soluble immunogenic dimer and effective to induce an anti-self IgE response in any mammal such as human is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Given the indefinite number of undisclosed immunogenic polypeptide, it is unpredictable which undisclosed immunogenic polypeptide would be useful for inducing even anti-self IgE response in a mammal, let alone treating *any* infection. Since the IgE sequence from non-

placental mammal in the immunogenic polypeptide is not enabled, it follows that any non-self domains such as CH2, CH4 domains of any non-placental mammal of the immunogenic polypeptide as set forth in claims 25-26, 28-34 and 36-40 are not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 1/13/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) a person having ordinary skill in the art would have been able to make a polypeptide containing both an IgE CH3 domain from a particular mammal (a self IgE CH3 domain) and one or more IgE domain from any other mammal (non-self IgE domains). A person having ordinary skill in the art at the time the application was filed in 1998 would have been able to obtain IgE sequences from any species using routine methods such as PCR or library screening techniques. (2) A person having ordinary skill in the art would have been able to add any amino acid sequence to the immunogenic polypeptide. (3) Claims 25 and 33 have been amended to recite that the polypeptide consists essentially of a self-IgE domain and one or more non-self IgE sequence present in a non-placental mammal. Claim 33 also requires at least one of the non-self IgE domains to contain an IgE sequence present in a non-placental mammal.

However, the specification does not teach how to make and use *any* immunogenic polypeptides mentioned above wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* "non-placental mammal" for inducing anti-self IgE response because the specification discloses only IgE polypeptide such as CH2 domain from opossum, or platypus and IgE CH4 domain from opossum or wombat. Even if the non-self IgE domains (IgE sequence) are limited to the specific non-placental mammal such as oposuum, platypus, and wombat, it is noted that the IgE sequence of platypus diverges from the IgE sequence (diverges) of other members of the non-placental mammal such as opossum, and wombat (See Figure 2, in particular). Thus it is clear that not all IgE sequences in non-placental mammal are similar, let

alone capable of inducing anti-self IgE response in *any* mammal. Further, there is no disclosure about the IgE sequence from other non-placental mammal such as koala, kangaroo, and wallaby. Given the divergent of IgE sequence among the non-placental mammal, there is insufficient guidance as to the structure such as the amino acids of the IgE sequence from any other non-placental mammal. Further, the term "comprises" is open-ended. It expands the non-self IgE domains to include additional amino acid at either or both ends. There is no guidance in the specification as to what type and number of amino acids can be added and whether the polypeptide having extra amino acids would retain both structure and function such as stabilizes the functional conformation of the self-IgE CH3 domain since the CH3 domain is critical for IgE binding to the high affinity FcεRI. Finally, there is insufficient working example demonstrating that any undisclosed immunogenic polypeptide consisting essentially of any self IgE CH3 domain and one or more non-self IgE domains comprises any IgE sequence present in any undisclosed non-placental mammal is effective to induce an anti-self IgE response in any mammal such as human. Without sufficient guidance, the immunogenic polypeptide that would be capable of dimerizing to form a soluble immunogenic dimer and effective to induce an anti-self IgE response in any mammal such as human is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Because of the lack of guidance as to the structure of any non-self IgE domain such as any IgE sequence present in any other non-placental mammal, a person skill in the art would not have been able to make, much less how to use any undisclosed immunogenic polypeptide for inducing anti-self IgE response in any mammal such as human.

5. Claims 25-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or

more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in any mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE, (2) the said immunogenic polypeptide wherein said mammal is a human, (3) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein said non-placental mammal is selected from the group consisting of opossum, platypus, koala, kangaroo, wallaby, and wombat, (4) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in any mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein said polypeptide is capable of dimerizing to form a soluble immunogenic dimer effective to induce said anti-self IgE response in said mammal, (5) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein one of said non-self IgE domains is an IgE CH2 domain, wherein one of said non-self IgE domains is an IgE CH4 domain and wherein said self IgE CH3 domain is located between said IgE CH2 domain and said IgE CH4 domain, (6) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in any mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein one of said non-self IgE domains is an IgE CH2 domain, (7) the immunogenic polypeptide, "consisting essentially of" *any* self IgE CH3 domain and *any* one or more non-self IgE domains, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in *any* non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any*

mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein one of said non-self IgE domains is an IgE CH4 domain, (8) *any* immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least N-terminal half of *any* self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in *any* non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal, (9) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least any N-terminal half of any self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in any non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in any mammal wherein the mammal is a human, (10) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least N-terminal half of *any* self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" any IgE sequence present in any non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal wherein said non-placental mammal is selected from the group consisting of opossum, platypus, koala, kangaroo, wallaby, and wombat, (11) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least any N-terminal half of *any* self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal wherein said polypeptide is capable of dimerizing to form a soluble immunogenic dimer effective to induce said anti-self IgE response in said mammal, (12) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least *any* N-terminal half of any self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal wherein one of said non-self IgE domains is an IgE CH2 domain, and (13) the immunogenic polypeptide, "consisting essentially of" one or more non-self IgE domains, and at least N-terminal half of *any* self IgE CH3 domain, wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in *any* mammal wherein one of said non-self IgE domains is an IgE CH4 domain.

The specification discloses only immunogenic polypeptides such as the ones shown in Fig 2 comprising a self IgE CH3 domain from rat, human, mouse, dog or pig and one or more non-self IgE domains such as IgE CH2 domain from opossum, or platypus and IgE CH4 domain from opossum or wombat for induce anti-self IgE response in a mammal.

With the exception of the specific immunogenic polypeptides such as the ones shown in Fig 2, there is insufficient written description about the structure associated with function of *any* immunogenic polypeptide because of the following reasons: the specification discloses only IgE polypeptide such as CH2 domain from opossum, or platypus and IgE CH4 domain from opossum or wombat. The specification does not disclose any other non-self IgE domains such as IgE sequence present in any non-placental mammal. Even if the non-self IgE domains (IgE sequence) are limited to the specific non-placental mammal such as opossum, platypus, and wombat, it is noted that the IgE sequence of platypus diverges from the IgE sequence (diverges) of other members of the non-placental mammal such as opossum, and wombat (See Figure 2, in particular). Further, the term "comprises" is open-ended. It expands the undisclosed non-self IgE domains to include additional amino acid at either or both ends. There is inadequate written description about the amino acids to be added and whether the resulting polypeptide having extra amino acids would retain both structure and function such as stabilizes the functional conformation of the self-IgE CH3 domain since the CH3 domain is critical for IgE binding to the high affinity FcεRI, in turn, effective to induce an anti-self IgE response in any mammal such as human or capable of dimerizing to form immunogenic dimer effective to induce anti-self IgE response in any mammal.

Further, the specification discloses only three IgE sequences from non-placental mammal such opossum, platypus and wombat, and given the divergent of IgE sequence of platypus from said other non-placental mammals, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 1/13/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) the written description requirement does not require all members of a genus to be described within a patent application, but rather that "a representative number of species" be described. (2) To further prosecution, independent Claims 25 and 33 have been amended to recite that the polypeptide consists essentially of a self-IgE domain and one or more non-self IgE sequence present in a non-placental mammal. Claim 33 also requires at least one of the non-self IgE domains to contain an IgE sequence present in a non-placental mammal.

However, the specification discloses only three IgE sequences from non-placental mammal such opossum, platypus and wombat. The specification does not disclose any other non-self IgE domains such as IgE sequence present in any non-placental mammal. Even if the non-self IgE domains (IgE sequence) are limited to the specific non-placental mammal such as oposuum, platypus, and wombat, it is noted that the IgE sequence of platypus diverges from the IgE sequence from other members of the non-placental mammal such as opossum, and wombat. Further, the term "comprises" is open-ended. It expands the non-self IgE domains to include additional amino acid at either or both ends. There is inadequate written description about the amino acids to be added and whether the resulting polypeptide having extra amino acids would retain both structure and function such as stabilizes the functional conformation of the self-IgE CH3 domain since the CH3 domain is critical for IgE binding to the high affinity FcεRI, in turn, effective to induce an anti-self IgE response in any mammal such as human or capable of dimerizing to form immunogenic dimer effective to induce anti-self IgE response in any mammal. Given that the lack of additional IgE sequences from non-placental mammal and the divergent of IgE sequence of platypus from other non-placental mammals such as opossum and wombat, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

6. The following new grounds of rejection are necessitated by the amendment filed 1/13/03.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 25-40 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The "consisting essentially of" in Claims 25 and 33 represents a departure from the specification and the claims as originally filed. The specification and the claims as originally filed do not provide a clear support for the said phrase and amendment now changes the scope of the immunogenic polypeptide. Applicant has not pointed out the support for said phrase in the amendment filed 1/13/03.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 25, 26, 28-34, and 36-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nissim *et al* (of record, EMBO J 10(1): 101-107, 1991; PTO 892) in view of US Pat No 5,653,980 (of record, Aug 1997; PTO 892), Keegan *et al* (Mol Immunol 28(10): 1149-54, Oct 1991, PTO 892), Presta *et al* (J Biol Chem 269(42): 26368-73, Oct 1994, PTO 892), Basu et al (J Biol Chem 269 268(18): 13118-13127, 1993; PTO 892) and Hellman *et al* (in New Horizons in Allergy Immunotherapy, Plenum Press, New York, 1996, pages 337-342; PTO 892).

Nissim *et al* teach various immunogenic chimeric IgE polypeptide such as CHM3 wherein the reference polypeptide consisting of a self IgE domain such as mouse IgE CH3 domain and one or more non-self IgE domains such as human IgE CH1, CH2 and CH4 domains (See page 102, chimeric human-mouse IgE, Fig 1, page 103, column 1, first full paragraph, in particular). The term "consisting essentially of" is still open-ended. It expands the claimed polypeptide to include additional amino acids at either or both ends to read on the reference polypeptide such a CHM3. Nissim *et al* teach that the reference immunogenic polypeptide wherein one of said non-self IgE domains are IgE CH2 and IgE CH4 domain and wherein said IgE CH3 domain is located between said IgE CH2 domain and said IgE CH4 domain. Nissim *et*

al further teach an immunogenic chimeric IgE polypeptide such as C3BX consisting essentially of one or more non-self IgE domains such as human IgE CH1, CH2 and CH4 domains and at least an N-terminal half of a self mouse IgE CH3 domain (See Figure 1, C3BX, in particular). Nissim *et al* teach that the entire C epsilon 3 domain in its native configuration is essential for binding of IgE molecule to the Fc epsilon receptor I and epitope to which the IgE bind should allow for the design of IgE analogue that can be used to block the onset of allergic response or to regulate IgE production.

The claimed invention in claim 25 differs from the teachings of the reference only that the immunogenic polypeptide consisting essentially of a self IgECH3 domain and one or more non-self IgE domains comprises an IgE sequence present in a non-placental mammal wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal and wherein said immunogenic polypeptide lacks a CH1 domain of IgE.

The claimed invention as recited in claims 28 and 36 differs from the teachings of the reference only that the immunogenic polypeptide wherein said non-placental mammal is selected from the group consisting of opossum platypus, and wombat.

The claimed invention as recited in claim 33 differs from the teachings of the reference only that the immunogenic polypeptide consisting essentially of one or more non-self IgE domains and at least an N-terminal half of a self IgE CH3 domain, wherein at least one of the said non-self IgE domains comprises an IgE sequence present in a non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal.

The claimed invention as recited in claims 29 and 37 differs from the teachings of the reference only that the immunogenic polypeptide wherein said polypeptide is capable of dimerizing to form a soluble immunogenic dimer effective to induce said anti-self IgE response in said mammal.

The '980 patent teaches a polypeptide comprising the amino acid sequence (the entire sequence or part thereof) of the constant CH2-CH3 domains of IgE that lacks the CH1 domain from mammalian species such as human and rat wherein the reference IgE domains are mutated by exchange (self versus non-self) fused to glutathione-S-transferase (Sj26) from *S japonicum* (See column 4, lines 21-26, column 9, lines 22-26, in particular). The reference polypeptide lacks light chain Ig sequences and the reference polypeptide is effective to induce anti-self IgE response in a mammal such as rat (See column 10, example 2, in particular). The term

"consisting essentially of" is still open-ended. It expands the claimed immunogenic polypeptide to include additional amino acids at either or both ends to read on the reference polypeptide. The '980 patent teaches that there is a risk that antibodies directed against the N-terminal part of the CH2 domain or the C-terminal part of CH3 domain may give rise to an anaphylactic shock in the mammals in which the antibodies are formed (See column 6, lines 36-39, in particular).

Keegan *et al* teach that the C epsilon 3 domain is important in the binding of mouse IgE to the murine B cell Fc epsilon RII as well as to the murine mast cell Fc epsilon RI; the presence of the C epsilon 4 domain influenced the binding of the recombinant IgE to the low affinity Fc epsilon RII (See abstract, in particular).

Presta *et al* teach that the Fc portion of IgE includes three domains Fcε2, Fcε3, and Fcε4 (See page 26368, column 2, in particular) and the C epsilon 2 and 4 domains of IgE are not involved in the binding of human and mouse IgE to the high affinity FcεRI (See page 26372, column 2, second full paragraph, in particular).

Basu *et al* teach that human IgE binds to the low affinity FcεRII in the Fcε2- cε4 domains (See page 13118, column 2, Figure 1, page 13121, column 1, in particular). Basu *et al* teach that the Fcε (329-547) contains only the cε3, cε4 domains exists in solution as a noncovalent dimer (See page 13122, line bridging the two columns, in particular). The reference immunogenic polypeptide such as Fcε2- cε4 domains is capable of dimerizing since it contains a cysteine residue at 328 in the Fc3 region, which is responsible for interchain disulfide bond.

Hellman *et al* teach a vaccination strategy by inducing a strong autoimmune antibody response against the patient's own circulating IgE using CH2 and CH3 domains of IgE coupled to foreign carrier (See page 338, last paragraph, in particular). Hellman *et al* teach that receptor binding region is located in the N-terminal part of the C3 domain and the entire CH2 and CH3 domains are used instead of short only short peptides from the N terminal region of the CH3 domain to obtain a larger number of surface epitopes and having these epitopes in close to native conformation (See page 339, first paragraph, in particular). Hellman *et al* further teach that in order to increase the immunogenicity of the polypeptide, the CH2-CH3 domain of IgE is fused to a foreign carrier such as S. japonicum GST polypeptide to circumvent the tolerance against the patient's own IgE (See page 339, in particular). Hellman *et al* teach that vaccination of the reference fusion protein is useful in decreasing serum IgE levels and blocking histamine release from mast cells and basophiles upon challenge with either a crosslinking polyclonal IgE or a specific allergen as a way to block the onset of allergic response (See page 337, Summary, in

particular). However, non-placental mammals such as opossum, platypus, and wombat are the most evolutionary distantly related mammals to placental mammals such as humans, rat and mouse and would be the most obvious choice as a source of distantly related non-self IgE. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Hellman *et al* teach that immunizing CH3-CH4 domain of self IgE is useful for inducing a strong autoimmune antibody response against the patient's own circulating IgE in decreasing serum IgE levels and blocking histamine release from mast cells and basophiles upon challenge with either a crosslinking polyclonal IgE or a specific allergen as a way to block the onset of allergic response (See page 337, Summary, in particular). Nissim *et al* teach that the entire C epsilon 3 domain in its native configuration is essential for binding of IgE molecule to the Fc epsilon receptor I and epitope to which the IgE bind should allow for the design of IgE analogue that can be used to block the onset of allergic response or to regulate IgE production. Keegan *et al* teach that the C epsilon 3 domain is important in the binding of mouse IgE to the murine B cell Fc epsilon RII as well as to the murine mast cell Fc epsilon RI; the presence of the C epsilon 4 domain influenced the binding of the recombinant IgE to the low affinity Fc epsilon RII (See abstract, in particular). Presta *et al* teach that the Fc portion of IgE includes three domains Fcε2, Fcε3, and Fcε4 (See page 26368, column 2, in particular). Basu *et al* teach that human IgE binds to the high affinity Fcε2- cε4 domains (See page 13118, column 2, Figure 1, page 13121, column 1, in particular). One having ordinary skill in the art would have been motivated to exclude the CH1 domain of IgE Fc epsilon because only CH2-CH4 domains of IgE are involved in IgE binding to its high and low affinity receptors on mast cells and basophiles as taught by Nissim *et al*, Keegan *et al*, Presta *et al* and Basu *et al* and the '980 patent teaches that there is a risk that antibodies directed against the N-terminal part of the CH2 domain or the C-terminal part of CH3 domain may give rise to an anaphylactic shock in the mammals in which the antibodies are formed (See column 6, lines 36-39, in particular).

11. Claims 27 and 35 are free of prior art.

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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